Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing reply, claims 1-7 are pending in the application, with claim 1 being the independent claim.

Based on the following remarks, Applicant respectfully requests that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections under 35 U.S.C. § 112

The Examiner has maintained his rejection of claims 1-7 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Paper No. 17, page 2.

The Examiner states that the claims are rejected because "the applicant has not shown that the claimed method would be effective in identifying potential vaccines for any infectious disease . . . [t]he application neither identifies any host cell gene products, nor provides any examples of such gene products identified by the claimed method, that have been shown to be potential vaccines." Paper No. 17, page 3.

Applicant asserts that ample guidance is provided in the specification for identifying potential vaccine targets. For example, the specification provides numerous examples of infectious agents which may induce differential expression of host cell gene products. *See e.g.* page 8, line 8 to page 9, line 24. These infectious agents include human immunodeficiency virus (HIV) and measles virus. *See* Specification, page 8, lines 8-9 and

page 9, line 11. Methods of determining differential expression of host gene products are discussed at pages 15-18, 20-22, and 28-30. Methods of determining immunogenicity of differentially expressed gene products are discussed at pages 22-24, 27-28, and 34-35.

Applicant has described specific strategies and methods of identifying host cell gene products upregulated or induced by infection with HIV. The specification discloses methods of identifying differentially expressed gene products utilizing specific cell lines modified to establish a high frequency of HIV infection and enhance the level of HIV infection. *See* Specification, pages 27-30. Utilizing these methods, Applicant has identified specific clones, two of which correspond to the genes encoding for CTP synthetase and tricarboxylate carrier. Northern blot analysis indicates that the expression of these two genes is significantly upregulated in cells following HIV infection. Specification, page 25, lines 21-28 and Figure 2. Finally, the specification also describes methods of determining immunogenicity of host cell gene products induced upon HIV-1 infection using both transgenic mice and human dendritic cells. *See* Specification, pages 33-35.

Compliance with the enablement requirement does not turn on whether a working example is disclosed. An example may be a "prophetic" example, that is, one that describes an embodiment of the invention based on predicted results rather than work actually conducted or results actually achieved. An applicant need not have actually reduced the invention to practice prior to filing. M.P.E.P. 2164.02; In *Gould v. Quigg*, 822 F. 2d, 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987). In the instant case, the lack of a working example showing actual immunogenicity is not probative of non-enablement.

Applicant points out that evidence in the art strongly indicates that Applicant's working examples can be utilized successfully to identify vaccine targets. Applicant submits

herewith Hickman *et al.*, *Journal of Immunology*, *171*: 22-26 (2003) (Exhibit A) and Herberts *et al.*, *Human Immunology*, *64*:44-55 (2003) (Exhibit B). These references show that the claimed method can be successfully used to screen infected cells for host cell gene products which are potential vaccine targets.

Hickman *et al.* identifies 15 host proteins, identified by mass spectrophotometric analysis, that are differentially upregulated and presented on HIV-infected human T cells. These host peptides include peptides derived from such proteins as high mobility group protein 1 (HMG-1), RNA polymerase II, eukaryotic translation initiation factor (eIF) 4GI, ubiquitin-specific protease 3 (USP3), heat shock protein 27 (hsp27), and tailless-complex protein (TCP)-1. Hickman *et al.* at page 24. These proteins, encoded by their respective genes, are involved in well-known processes such as RNA transcription and translation, protein degradation, and protein folding. The peptides were identified after elution following the harvest of B*0702/peptide complexes, indicating that these peptides are characterized by their ability to bind one of the major classes of MHC Class I molecules.

Hickman *et al.* states that "the analysis of HLA-B*0702 repertoire after HIV infection reveals a series of host-protein-derived peptides presented uniquely by infected cells." Hickman *et al.* at 26. They conclude that the mechanism by which virus-induced host epitopes could function in the induction of autoimmune responses directly through increasing the concentration of self peptides on the cell surface is "supported by a recent study demonstrating autoreactivity following measles virus-induced up-regulation of self peptides." Hickman *et al.* at 26.

Herberts *et al.* identifies two abundant self peptides that are induced or upregulated following measles virus (MV) infection: IFI-6-16_{74-82} and Hsp $90\beta_{570-578}$. IFI-6-16_{74-82} is a

peptide derived from the type I interferon inducible protein; Hsp $90\beta_{570\text{-}578}$ is a peptide derived from the β chain of heat shock protein 90, an abundant cytosolic chaperon protein essential for the viability of eukaryotic cells which is upregulated under stress conditions such as heat shock and inflammation. These peptides were identified by subtractional analysis after elution of HLA-A*0201/peptide complexes of cells prior to and 48 hours after MV infection. Herberts *et al.* at page 47.

Herberts *et al.* note that their results, combined with the findings of other groups, show that "both acute and chronic viral infections can lead to the upregulation or induction of self-peptides in MHC molecules." Herberts *et al.* at page 54.

The disclosure of Applicant's claimed invention clearly shows that the claimed method would be effective in identifying potential vaccines. Applicant's disclosure is corroborated by the results of Hickman *et al.* and Herberts *et al.* which identify genes that are upregulated following HIV and measles virus infection. Both of these infectious agents are also specifically disclosed in Applicant's specification as agents which induce differential expression of host cell gene products.

Furthermore, Herberts *et al.* also indicates that virus-induced host epitopes can function in the induction of autoimmune responses, and both articles describe peptides which are characterized by their ability to bind to at least one major class of MHC molecule. The ability of these peptides to bind to MHC molecules and the potential of these peptides to induce autoimmune responses are factors which show that these peptides are clear targets for the immune system, and hence, potential targets for a vaccine. The results described above show that Applicant's claimed method would be effective in identifying potential vaccines.

Based on the above remarks, Applicant's respectfully request that the rejection of claims 1-7 under 35 U.S.C. § 112, first paragraph be withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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